Attorney Docket No.: 8920-000005

COURTESY COPY FOR EXAMINER IRENE MARX—NOT FOR FILING

REMARKS

Claims 3 and 6-12, as amended in previous papers and herein, and new claims 13-18 are pending in the application. Applicants thank Examiner Marx for the courtesies extended in the interview with Applicants' attorney on April 29, 2003.

Applicants request reconsideration and withdrawal of the rejection of claims 3 6-12 under 35 U.S.C. § 103(a) because the P.T.O. has not established a *prima facie* case for obviousness as required under recognized patent practice and procedure as well as by case law. To establish a *prima facie* case for obviousness, the P.T.O. must show that all claim limitations are taught or suggested. M.P.E.P. § 2143.03; *In re Royka*, 180 USPQ 580 (CCPA 1974); *In re Wilson*, 165 USPQ 494, 496 (CCPA 1970) ("All words in a claim must be considered in judging the patentability of that claim against the prior art."). In the present Office Action, the P.T.O. cites Sengupta *et al.* (1990) taken with Kubicek *et al.* to support the rejection. The P.T.O.'s rejection is based, in part, on the statement on page 2 that "In view of the similarity of the metabolic pathways involved in the biosynthesis of cellulolytic enzymes, including enzyme preparations containing high cellobiase, in fungi one of ordinary skill in the art would have had a reasonable expectation of success in obtaining a similar improvement in the stability of the excreted cellobiase produced, at least when using 50 μg/ml tunicamycin or 2-deoxy-D-glucose in the process (See, e.g., Kubicek et al, page 398, col 2)." Applicants respectfully submit that the Examiner's interpretation of Kubicek is incorrect. Kubicek, on page 398, col 2, states that "Recently Merivuori *et al.* (1985) reported, based on experiments using the N-glycosylation specific inhibitor tunicamycin, that N-linked glycosylation is not necessary for cellulase secretion, but it improves the stability of the secreted protein in *T. reesei*." The Examiner has apparently interpreted the word "it" in the final phrase of that sentence as referring to tunicamycin. While that is facially a possible interpretation, an examination of the Merivuori reference (copy enclosed) reveals that "it" refers to N-linked glycosylation rather than tunicamycin. For example, Merivuori states in the

Attorney Docket No.: 8920-000005

COURTESY COPY FOR EXAMINER IRENE MARX—NOT FOR FILING

Summary that "Endoglucanase activity in culture broths from tunicamycin grown mycelia was more thermolabile and protease-sensitive than the same activity from control cultures." If Kubicek is read in light of Merivuori, Applicants suggest that is not possible to interpret Kubicek as reciting that tunicamycin improves the stability of the secreted protein in *T. reesei*. Applicants, therefore, submit that neither Kubicek nor Sengupta, either separately or in combination, would lead one of ordinary skill in the art to have had a reasonable expectation of success in obtaining an improvement in the stability of excreted cellobiase in the presence of a glycosylation inhibitor, and respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

In a previous response to an Office Action, Applicants submitted that Kubicek should be withdrawn as a reference, because it does not disclose the production of cellobiase in the presence of a glycosylation inhibitor, pointing out that Kubicek is a study of endoglucanase, an enzyme distinct from cellobiase. In the present Office Action, the P.T.O. states that "it is admitted that Kubicek discloses that the 'production and secretion of cellobiase in *Trichoderma reesei*' was studied in presence of glycosylation inhibitors." Without conceding that there is an admission, applicants nonetheless point out that Kubicek is a study of inhibition of glycosylation in non-growing mycelia and protoplasts of *Trichderma reesei*. (See, e.g., first sentence of the abstract). In contrast, the present application is directed to enhancement of cellobiase activity of *Termitomyces clypeatus* in growing mycelial cultures. (See, e.g., page 5, first paragraph). Hence, in order to reach a favorable conclusion of prosecution of this application, Applicants have amended Claim 3 to reflect this distinction.

In the present office action, the P.T.O. states that the specification provides on page 9 for a range of 0.05-2 mg/ml for glycosylation inhibitors. In order to reach a favorable conclusion of prosecution of this application, Applicants have amended Claim 3 to recite a range of from about 10 μg/ml to-about 2 mg/ml, the lower figure being found at least page 9 table 1, regarding an increase in cellobiase activity (compared to control) observed in the presence of 10 μg/ml tunicamycin. Furthermore, in response to the P.T.O.'s

COURTESY COPY FOR EXAMINER IRENE MARX—NOT FOR FILING

contention that no clear definition of "high" activity is found in the as-filed specification, claim 3 has been amended to indicate that cultures with high activity exhibit an increase in cellobiase activity with respect to control cultures that are not treated with a glycosylation inhibitor.

The P.T.O. states that arguments by counsel in the Supplemental Response previously filed regarding regulation of by catabolic repression of extracellular secretion vs. production of cellobiase have not been substantiated with appropriate evidence. Furthermore, the P.T.O. states in response to an argument put forth in the Supplemental Response that it notes that the present invention recognizes that 2-deoxyglucose acts *in vivo* as a glycosylation inhibitor, but that the independent claim is directed to the use of any glycosylation inhibitor. In order to hasten favorable completion of prosecution, applicants respectfully withdraw, without prejudice, these arguments from consideration in this paper.

In Claim 3, reference to a method for producing an enzyme preparation from a growing culture of *Termitomyces cypeatus* is supported at least by Claim 3 as originally filed and on page 5, lines 2-11; support for a sterilized medium containing from about 10 μg/ml to about 2 mg/ml can be found at least on page 9, table 1 (2nd and 7th entries); support for growing the mycelial culture can be found at least on page 5, line3; support for enzyme preparation containing high cellobiase activity that is increased in comparison to cellobiase activity produced by the same organism under the same conditions in absence of the glycosylation inhibitor can be found at least on page 9, tables 1 and 2.

In Claim 8, support for 1-deoxynojirimycin can be found at least in Claim 8 as originally filed and on page 9, table 1.

In Claim 13, support for an enzyme preparation containing high cellobiase activity is an enzyme preparation containing cellobiase activity that is at least about 2.2 units/ml and for a sterilized medium contains about 0.05 mg/ml 2-deoxy-D-glucose can be found at least on page 9, table 1 (4th entry).

Attorney Docket No.: 8920-000005

COURTESY COPY FOR EXAMINER IRENE MARX—NOT FOR FILING

In Claim 14, support for an enzyme preparation containing high cellobiase activity is an enzyme preparation containing cellobiase activity that is at least about 50 units/ml and for a sterilized medium contains about 1 mg/ml 2-deoxy-D-glucose can be found at least on page 9, table 1 (5th entry).

In Claim 15, support for an enzyme preparation having cellobiase activity that is at least about 90 units/ml, wherein the sterilized medium contains about 300 μg/ml 2-deoxy-D-glucose can be found at least on page 9, table 2 (3rd entry).

In Claim 16, support for an enzyme preparation having cellobiase activity that is at least about 140 units/ml, wherein the sterilized medium contains about 1 mg/ml 2-deoxy-D-glucose and further contains about 500 μg/ml mannose can be found at least on page 9, table 2 (4th entry).

In Claim 17, support for an enzyme preparation having cellobiase activity that is at least about 6.18 units/ml, wherein the sterilized medium contains at least about 2 mg/ml glucono-lactone can be found at least on page 9, table 1 (7th entry).

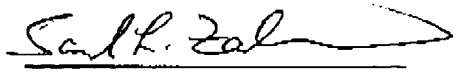
In Claim 18, support for an enzyme preparation having cellobiase activity that is at least about 1.4 units/ml, wherein the sterilized medium contains at least about 80 μM 1-deoxynojirimycin can be found at least on page 9, table 1 (3rd entry).

It is believed that the claims are in a condition for allowance and such favorable action is respectfully requested. If, however, any of the claims are deemed by the P.T.O. not to be in a condition for allowance, Applicants request an interview with the P.T.O. so that any remaining issues can be resolved. Should any questions arise, the P.T.O. is requested to contact the undersigned attorney.

Attorney Docket No.: 8920-000005

COURTESY COPY FOR EXAMINER IRENE MARX—NOT FOR FILING

Respectfully submitted,



Saul L. Zackson, Ph.D.
Reg. No. 52,391
Harness, Dickey & Pierce, P.L.C.
7700 Bonhomme, Suite 400
St. Louis, Missouri 63105
(314) 726-7500